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New Concepts in Cancer Control

Preventable and Avoidable Cancers

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THE HONOR OF GIVING the L. Henry Garland Memorial Lecture is one which I have cherished because of my long friendship with this dynamic, effervescent and inspiring man. Harry and I were contemporaries in radiology. It was my privilege not only to nominate him for the presidency of the American College of Radiology, but also to be one of his sponsors for its gold medal.

Rather than eulogize Harry, which has been done so beautifully by his great and good friend, Dr. Dwight Wilbur[1] and by our colleague, Dr. Philip Hodes,[2] I am going to tell you about some of my personal experiences with this exceptional man. In the later years of his phenomenal career we worked together very closely when our interests became focused on the problems of cancer control. We both became involved in the American Cancer Society, Harry as a member of the National Advisory Committee on Research on the Therapy of Cancer and I as chairman of the national Medical and Scientific Committee.

Harry had an intuitive sense—almost an instinct—for penetrating the heart of a problem and arriving at a decisive opinion. It was either black or white and one which he would vigorously defend against all challenges. Yet, if further debate developed a more constructive or more certain approach, he would accept it. Later, when I became a member of the Editorial Board of *CA* and then editor of *Cancer,* the mail almost every week contained a brief, concise and spirited note either commending or criticizing a particular article or issue. If in his opinion an article had overemphasized the efficacy of a surgical procedure or failed to give radiation therapy its just position in the management of that malignant disease, he would suggest a counterattack by developing an article on the effectiveness of radiation treatment. I have missed these spicy and sometimes jolting notes, for they always stimulated a responsive action. To him we owe a great debt for his fearless, unflinching and courageous efforts to help establish the place of radiation therapy in the management of cancer. It is most appropriate that the California Radiological Society has dedicated this lectureship to memorialize the indomitable and flaming spirit of L. Henry Garland, a man of incessant energy and devotion to the advancement of radiology. I have chosen for this lecture the title "Preventable and Avoidable Forms of Cancer," because the field of cancer prevention intrigued Harry and because it offers greater possibilities for the control of cancer and the saving of lives than any other measure at our command today.

The magnitude of the problem and the possibilities of achieving success become apparent when we realize that 16 percent of the deaths from all causes in the United States are due to cancer. The age-adjusted death rate from cancer per 100,000 population has increased from 112 in 1940 to 128 in 1965. This year (1969) about 325,000 persons will die of cancer, about 900 each

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day. Of every six deaths, one is from cancer. About 940,000 Americans will be treated for cancer, newly diagnosed in 615,000 of them. Of Americans now living more than 50,000,000 will eventually have cancer—one in four of us; and two of every three families will have an experience with it.

On the bright side 1,500,000 Americans are alive today who have been cured of cancer for at least five years—one out of every three have survived. The majority of cancer deaths occur in persons over 65 years of age. In women age 30 to 54 it is the leading cause of death. Since 1949 more males die of cancer than females, largely due to the increase in lung cancer. In 1969 the ratio will be 55 males to 45 females.

The leading sites of cancer causing death in males are: to age 34, the blood; age 35 to 75, the lung; 75 and over, the prostate. In females the ranking is: under age 15, leukemia; age 15 through 34, the uterus; 35 to 74, the breast; age 75 and over, the colon and rectum.

In children cancer deaths are exceeded only by accidents—causing 4,000 deaths under age 15, about half of them from leukemia. Today there are more than 300,000 children under 18 who have lost their fathers from cancer and 250,000 who have lost their mothers.*

These are the stark realities. This is why the prevention of cancer should concern us. As radiologists we see more patients with cancer than any other medical specialty. In diagnostic radiology the large majority of the examinations are concerned with identifying the presence of cancer or in ruling it out. More than 50 percent of all cancer patients will at some time undergo radiation treatments. Radiologists should be among the leaders in initiating cancer detection programs, in supporting measures for controlling carcinogenic pollutants in the atmosphere, in the water and in the earth. They should actively support legislative and public health measures designed to study possible carcinogens in food preservatives and additives, in fungal contaminates and in cosmetics and medicinal preparations. They should support measures for the control of unnecessary radiation exposure as well. There are unlimited opportunities to provide leadership to volunteer cancer and other health agencies, to appropriate committees in organized medicine, to governmental health advisory councils and to those of the National Institutes of Health in the development of effective programs for cancer control. Above all, we should set the example for our medical colleagues, for our patients and for our friends by refraining from indulging in the use of known carcinogens.

Sir Alexander Haddow[3] when president of the Ninth International Cancer Congress in 1966, stated: "It would appear that the majority of human cancers are avoidable"—these are the cancers that are influenced by extrinsic environmental factors, directly or indirectly. They include many tumors of the respiratory system; the gastrointestinal and urinary tracts; the skin and mouth; the hormone dependent organs such as breast, thyroid and uterus, and the blood and lymphatic systems. These are the cancers that I refer to as preventable and avoidable cancers and cancers arising from personal indifference.

The "Class Consciousness" of Cancer

Socio-economic factors also exert a strong influence on the control of this group of cancers. Breslow[4] in a study of the California Tumor Registry demonstrated what he calls the "class consciousness" of cancer and its treatment, namely that:

1. Cancer of the cervix is twice as frequent in the lowest income group as in the highest.
2. Among men, lung and stomach cancer strikes the lowest income group twice as frequently as it does those with the highest income.
3. Only one-third of the cancer patients in county hospitals had received the benefits of early diagnosis while one-half of those in private hospitals received these benefits.
4. Sixty-two percent of private hospital patients with cancer of the cervix survived five years or more but only 39 percent of the county hospital patients.
5. Alameda County reported two-thirds of the women in the highest social class had received at least one Papanicolaou test while only one-third of those in the lowest economic group had received such a test.

It is unfortunate that the largest portion of the population should benefit the least from cancer control measures. This imbalance must be corrected by new and expanded programs.

The identification of environmental factors that have a causal relationship in the development of cancer and the elimination or protection against

*All cancer statistics taken from "1969 Cancer Facts and Figures." Published by the American Cancer Society, Inc., 219 East 42nd Street, New York, N.Y. 10017.

them can provide a short cut for the control of many cancers. The classical example and the first identification of an environmental chemical causative agent of cancer in man was cancer of the scrotum. It was a common occurrence among chimney sweeps, nearly 100 times more frequent than in the general male population, and was caused by their years of contact with soot. When this was recognized by Sir Percival Pott[5] in 1775, protective clothing and cleanliness were instituted and this avoidable cancer has practically disappeared.

The most common of all cancers, cancer of the skin, is an avoidable cancer. It is induced by prolonged over-exposure to sunlight, to ultraviolet lamps, to arsenic, to certain oils and chemicals, all of which agents it is possible to avoid, and thus to prevent this form of cancer. Because it occurs on the skin, it is easily seen, recognized early, promptly treated and cured. The cure rate for skin cancer is 93 percent in the United States, but because of the high incidence the 7 percent failures account for over 4,000 unnecessary deaths every year.[6]

Industrial Prevention Programs

Large industries were among the first to recognize the value of cancer prevention programs. For example, Eckardt,[7] the director of the Medical Research Division of Esso Research and Engineering Company of New Jersey, instituted a cancer detection examination at the time of the employees' periodic health check-up and provided prompt treatment of any malignant or pre-malignant lesions found. The company constantly studies working conditions to eliminate the possible exposure of workers to carcinogens in that industry. So successful has been this program that after 20 years the company has not had a single case of cancer that could be attributed to oils. In the beginning they found that cancer to the scrotum was developing in some of their wax pressmen—in 11 among 77 of them. As these men worked at their tables they pressed the frames containing wax and oils into the crotch of their pants, which became saturated with these materials. This practice was stopped, the men were required to take showers at the end of the day and to wear a clean uniform daily, and there has been no further incidence of this particular cancer.

Another preventable cancer occurred in the bladder of upwards of 70 percent of the chemical workers that were heavily exposed to aniline dye intermediates, and especially to betanaphthylamine.[8] When this chemical was identified as the culprit and exposure to it was stopped, this particular cancer disappeared and the overall incidence of bladder cancer in this group of men returned to normal. Wynder and associates[8] showed that cancer of the bladder is predominantly a male disease, that it is increasing in some countries, including the United States, and that cigarette smoking increases the risk of bladder cancer by about two-fold. They also pointed out that shoe repairers appear to have an inordinately high incidence of bladder cancer and that they should be advised to handle dyes and polishes with more care, and to wash their hands frequently with soap and water as a means of reducing their higher risk. Another lead is the recent report by Bouser[9] that about 50 percent of all patients with bladder cancer have abnormal tryptophan metabolites in their urine—an important observation that is being investigated.

It has long been known that about 50 percent of the miners in the pitchblende mines in Joachimsthal[10] and about 75 percent of the miners in Schneeberg,[10] both in Czechoslovakia, dying from natural causes, died from cancer of the lung brought about by prolonged exposure to radioactive ores. A similar high incidence of lung cancer has appeared among the uranium miners in the Colorado plateau due to their excessive inhalation of radon gas.[11,12] By periodic cytologic examination of the sputum of these miners, it is possible to detect the presence of abnormal cells that are believed to be the precursers of malignant changes in the bronchial mucosa. When such cells appear in the sputum of a miner he is removed from the mine, given a job above ground, and instructed to stop smoking. Usually the cells in the sputum will slowly return to normal, and presumably he has avoided development of a pulmonary cancer.

Among chromate ore workers the estimated lifetime incidence of lung cancer was approximately 35 percent.[13] Workmen who inhaled beryllium salts and oxides[14] also had a higher incidence of lung cancer. The inhalation of asbestos fibers[15] is known to be a responsible agency in the causation of lung cancer as well as of malignant mesotheliomas of the pleura and peritoneum. Even the inhalation of a small amount of asbestos fibers[16] seems to be capable of giving rise to these malignant tumors.

In the 1930s fatal bone cancers appeared in women who had ingested minute quantities of

radium over the years by habitually "pointing" their brushes in their mouths as they painted luminous dials on watches and instruments. These were accidentally induced cancers which are now avoided.

It is a curious but well established fact that the incidence of cancer of the ethmoid sinuses is high among men refining nickel ores.[13] Another substance, cobalt,[13] when accidentally injected or thrust beneath the skin almost invariably caused a cancer to develop at that site. Fortunately, exposure to all these carcinogenic substances can and is being eliminated by modern protective industrial practices and these cancers avoided.

The most important environmental causal agent in the production of internal cancer today is, of course, the prolonged inhalation of cigarette smoke. The Second Report of the Surgeon General of the United States Public Health Service, "The Health Consequences of Smoking," issued in 1967, reviewed more than 2,000 additional research studies, all done since the 1964 report. They confirmed and strengthened the conclusions of the initial report that the inhalation of cigarette smoke was the major cause of lung cancer, and in addition brought out:

1. That a "substantial" increase occurs in the mortality ratios for smokers, especially cigarette smokers, from cancer of the oral cavity and pharynx.

2. That "cigarette smoking is a significant factor in the causation of cancer of the larynx."

This latter conclusion was strengthened by von Essen and associates[17] who in December 1968 reported on "Cancer of the Larynx in Connecticut." For the period 1935-1959 there were 1,438 cases with a male to female ratio of 12:1. The annual age-adjusted incidence for laryngeal cancer rose from 3.8 to 6.1 per 100,000 males during this 25 year period—a rise paralleling the spiralling incidence of lung cancer.

The smoking problem can be summarized by saying it is tragic that the medical profession and the public have been so long in recognizing that cancer of the lung is largely an avoidable cancer and that cancer of the oral cavity, pharynx and larynx probably belongs in this category. These cancers for the most part are, then, due to the personal indifference of the individual.

As recently as ten years ago or even five years ago, how many physicians would have predicted that today cancer of the cervix would be considered an avoidable cancer? Twenty years ago this cancer was the No. 1 killer of women. In the last 25 years the death rate from cervical cancer has dropped 50 percent. The widespread application of the "Pap" test, named after the late Dr. George Papanicolaou, has made this possible. By this test cancer can be found in its earliest stages, before it becomes invasive, before it can be seen by the naked eye, and at a time when it is practically 100 percent curable. Yet after 25 years it is estimated that 60 to 70 percent of the adult female population are still unscreened—30 to 40 million women.

The effectiveness of the "Pap" test in the control of cervical cancer has been demonstrated in Louisville, Kentucky,[18] where Pap smears have been done on a large group of women for the past ten years. For the last seven years not one single case of invasive cancer of the cervix has appeared among these women, proving that yearly cytological screening provides essentially 100 percent protection. Today one can say that a death from cancer of the cervix is a preventable death. It need only occur from personal indifference or self-neglect.

It may also be considered an avoidable cancer as well, for cervical cancer has a much higher incidence in countries where adequate personal hygiene is difficult to obtain, such as in the countries of Latin America, India, China and Africa, and has the lowest incidence in countries in which the plumbing facilities are better. In Singapore it was demonstrated that those women who have access to a private bathroom have a lower incidence of cervical cancer than those who do not. It is twice as high in women who marry at 16 years of age or younger and who initiate sexual intercourse at an early age. It occurs more frequently in married than in unmarried women. In women married twice or more, the incidence jumps about three times. Prostitutes have a very high incidence.

In studies of 13,000 nuns in the Province of Quebec, of 100,000 nuns in the United States, and of nuns in several European countries, no cervical cancers were found or no deaths from cervical cancer were reported,[19] indicating that cervical cancer is very rarely found in the absence of sexual intercourse. In contrast, however, Wynder found that nuns had cancers of the body of the uterus, of the ovary and of the breast, and that the incidence of endometrial cancer in them was higher than in the average female population.

A somewhat related and another avoidable cancer of the penis—related because wherever the incidence of cancer of the cervix is low, so is the incidence of penile cancer, and where one is very common, so is the other. Penile cancer is probably the oldest of avoidable cancers. It has been almost non-existent among the Jews in whom circumcision is performed at the end of the first week after birth as part of a religious rite. In Moslems circumcision is carried out before puberty, and they also have a low incidence of this cancer. In a series of 120 cases of this cancer at New York Memorial Hospital for Cancer and Allied Diseases, Dean[20] reported that none of the patients had been circumcised in infancy It has also been established that circumcision after the age of puberty is ineffective. In a country as health conscious as the United States, this cancer could be largely eliminated by circumcision and personal cleanliness. Where these practices are neglected, the incidence is considerably higher, as in Ceylon, South Africa and Latin America. In India it may account for as much as 10 percent of all cancers in males and, in China up to 20 percent. Mexico may have the world's highest known incidence of this disease. In the United States it amounts to from 1 to 3 percent of all cancer[20]

Cancer Related to Social Customs

The social customs that can lead to cancer are complex, deeply rooted, and apparently satisfy strong human desires. For example, the Cancer Institute of Madras in India[21] reports that 48 percent of all malignant neoplasms were oral or pharyngeal in origin, with more than 20 percent of them arising from the buccal mucosa. In contrast buccal cancers in the United States account for only 4.6 percent in males and 1.7 percent in females.[21] The high incidence of intraoral cancers also prevails in the Philippines, Ceylon, Burma, Pakistan, Guam and Russia and is most frequent in the low income groups there. It is probably related to the national habit of chewing a mixture of tobacco and slaked lime with betel nut. This "quid" is placed in the chewer's mouth between the cheek and the gum and kept there most of the day. It stains the teeth and keeps the mouth filthy. These "self-induced" cancers are pitiful to see.

A similar habit exists in the southeastern United States. It is "snuff-dipping," and is fairly common, especially among the older women in the low income groups. Snuff is no longer sniffed into the nose as was fashionable in the 18th century. Today a pinch of this flavored, powdered tobacco is placed in the gingival buccal gutter. The prolonged contact of the quid with the limited area of mucosa produces a severe chronic local irritation that is an ideal environment for any carcinogen in the mixture to exert its effect by direct contact.[22]

Snuff dippers' intraoral cancers are not just a casual or freak occurrence. Brown and associates,[23] of Atlanta, recently reported on 394 cases of oral cancer in which 78 percent occurred in the buccal gutter and were in women. Seventy-five percent of these women were confirmed snuff users and kept the quid at that location. Rosenfeld and Calloway,[24] reporting from Nashville, Tennessee, found that 90 percent of the women in a group with 525 intraoral cancers had carcinoma of the gingiva-buccal area and were habitual users of snuff. In contrast are reports from Buffalo, the Mayo Clinic, and New York City, in which cancers of the oral cavity and pharynx occur about five times more frequently in men than in women.[25,26,27]

Cancer of an unusual type that is suspected of having a causal relationship to environmental factors is Burkitt's sarcoma. It was first thought to be limited to African children, but more thorough studies revealed that it can appear in children of all races—American, European, Asian and Indian, but the strikingly high incidence occurs only in a zone across Central Africa with an elevation of less than 5,000 feet, an annual rainfall of more than 200 inches and a temperature that does not fall below 60 degrees Fahrenheit. These conditions raise the question: Could this type of cancer be due to a virus that was possibly transmitted by a vector such as a mosquito? Dorfman[28] suggested that the unusually high incidence in a particular area in Africa, the predilection for the bones of the jaw and face and the rarity of leukemic transformation may reflect an attendant host susceptibility in African children in addition to the environmental factors.

There is another group of cancers which appear to be related to causal factors in our environment, but the factors have not yet been identified. The first of these is cancer of the stomach, which has been undergoing a remarkable decline for the past 30 years in the United States for no known reason. At the same time cancer of the stomach has been increasing in Yugoslavia, Mexico, India, the Soviet

Union, Iceland and, particularly, in Japan, where it is the No. 1 cancer. Yet the Japanese who live in the United States do not have the same high incidence. Why? It might be related in some way to the low protein diet of these people, but this is not certain. The disparity in the incidence among these different peoples apparently lies in differences in their environmental food habits. It is now known that aflatoxin as produced by the fungus *Aspergillus Flavus* growing on spoiled peanuts is, according to Bouser,[9] among the most potent carcinogens known. It is believed to interfere with the synthesis of DNA. Aflatoxin has also been obtained from the fungus that grows on moldy rice. Since the poorer quality of these foods is more likely to be contaminated by such fungi and since the highest incidence of stomach cancer occurs in the lower income groups, it is easily understood why aflatoxins have become suspect and are under serious investigation.

Epidemiologists would like to know why American women have about seven times more cancer of the breast than Japanese women. They think that there is some connection in the length of time they spend in nursing their children, but much more research is needed into glandular and related functions to make sure. They would also like to know why cancer of the breast is more frequent in unmarried than in married women.

American Indians and Eskimos of both sexes are said to have a low cancer rate generally, for which there is no explanation. The Indian women, however, have a normal or higher mortality rate from cancer of the liver and uterus.

Cancer of the colon and rectum in the United States is the No. 1 internal cancer among men and women; 46,000 deaths will occur from it this year, and there will be 76,000 new cases. It is the only cancer in which the incidence is the same in both sexes. Yet in the same countries that have a high incidence of cancer of the stomach there is low incidence of cancer of the colon. It is infrequent in Mexico, Latin America, India and in Japan.

Haenszel[29] of the National Cancer Institute has shown that the incidence of cancer of the colon in people who live in urban communities is higher than in those dwelling in rural communities, and that there is an appreciably higher rate in people of the northern part of the United States than in those of the southern states. These findings remain consistent in migrants from the northern states to the southern states, and vice-versa, as well as migrants going to and from rural and urban centers.

It is interesting that colon cancer occurs only one-tenth as frequently among the members of the Bantu tribe in Southeast Africa as it does in the United States. Yet cancer of the liver which accounts for 50 percent of all cancer deaths among the Bantus, accounts for less than 4 percent in Europeans and North Americans.[30] Again a search must be made to identify environmental factors that account for these contrasting incidences. Scientists speculate that the Bantu tribesmen exist on a diet deficient in milk and meat, particularly in the early years, which predisposes them to cirrhosis of the liver, from which this form of cancer appears to develop. Here then is the opportunity to identify other environmental factors and add to the list of preventable cancers.

In Puerto Rico[30] the frequency of cancer of the esophagus is ten times higher than in upper New York State. The physicians in Puerto Rico strongly suspect that it is due to the practice among the lower socio-economic groups of drinking bad rum which they make in their homes.

Mention can only be made of the intricate problems of the carcinogenic potentials of pesticides, of food additives—such as colors, flavors, emulsifiers, antioxidants and fungal contaminants, although many are suspect. Likewise, cosmetics and certain medical preparations can only be mentioned, because they are very complex and much work needs to be done in this field. The Federal Drug Administration has taken an interest in these products and they are now under serious investigation.

The concept of avoidable cancers is not new, it has been utilized by industry for years. But what is new is that more of the factors that can induce cancer are being identified and that a continuing organized and intensified effort is in operation to detect new ones.

The concept of preventable cancers is relatively new, but it did not achieve important recognition until the Pap test was introduced and finally accepted. The recognition that means for the prevention of cancer can be developed, can be practical and can be applied to large populations has been a great achievement in the control of cancer. It cannot be foretold at this time what magnitude of cancers may fall into this group until more knowledge and the results of research are accumulated, but there will be many.

The concept that cancers can arise from personal indifference is new and one which deserves both professional and public acceptance.

With the understanding of these concepts, it becomes apparent that cancer is largely a social problem and that public health measures can be developed that could lead to the control of a majority of the cancers today. Cancer of the cervix has already been conquered. Cancer of the lung is reasonably understood, the major causal factors have been identified, and all that remains to eliminate 80 to 85 percent of lung cancers is to gain an acceptance of existing educational programs and to change the social complex that promotes the desirability of smoking. Cancer of the colon and rectum are slow to metastasize and the survival rate associated with them if treated before spread has occurred is high—70 percent. Annual sigmoidoscopic examinations for populations in western Europe and North America can provide for the detection of this cancer in more than 50 percent of cases at a stage when there is an excellent chance of cure. Fortunately increased interest and efforts are being directed to find the etiological factors involved in colon cancer. The answers may come from further epidemiological studies and geographic pathology. While we are awaiting the final solution of the cancer enigma that will come from further basic research, great efforts are justified for the full development of programs on avoidable and preventable cancers and those arising from personal indifference. For the past two decades the great emphasis has been on furthering cancer research, and rightly so. The time has now come to direct emphasis to the prevention and avoidance of cancer and to teach people that cancers can arise from self-neglect.

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